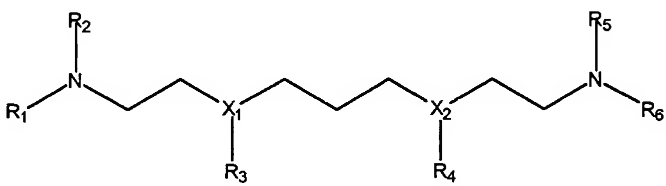
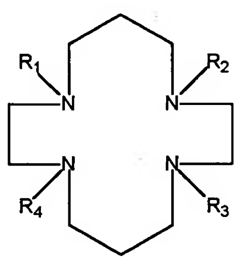
ABSTRACT

The invention relates to the preparation of novel therapeutically active polyamines, such as derivatives of 1,3-bis-[(2'-aminoethyl)-amino]propane (2,3,2-tetramine) and 1,4,8,11-tetraazacyclotetradecane (cyclam), optimization of their mechanistic and bioavailability characteristics, so these compounds can be used in the treatment of Parkinson's disease, Alzheimer's disease, Lou Gehrig's disease, Binswanger's disease, Olivopontine Cerebellar Degeneration, Lewy Body disease, Diabetes, Stroke, Atherosclerosis, Myocardial Ischemia, Cardiomyopathy, Nephropathy, Ischemia, Glaucoma, Presbycussis, Inherited Mitochondrial Neuropathies and Myopathies and Cancer.

Accordingly, in one aspect the invention is directed to compounds of the formula:



or



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wherein

R_1 and R_2 may be the same or different and are hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol, α-lipoic acid, α-tocopherol, ubiquinone, phylloquinone, β-carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene – $(CH_2)_n[XCH_2)_n]NH_2$ - wherein n = 3-6 and X = nitrogen, sulfur, phosporous or carbon, or heterocycle wherein R_1 and R_2 taken together are $-(CH_2XCH_2)_n-$ wherein n = 3-6 and X = nitrogen, sulfur, phosporous or carbon.

R_3 and R_4 may be the same or different and are hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol, α-lipoic acid, α-tocopherol, ubiquinone, phylloquinone, β-carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene or heterocycle wherein R_3 and R_4 taken together are $-(CH_2XCH_2)_n-$ wherein n = 3-6 and X = nitrogen, sulfur, phosporous or carbon.

R_5 and R_6 may be the same or different and are hydrogen, alkyl, aryl, cycloalkyl, amino acid, glutathione, uric acid, ascorbic acid, taurine, estrogen, dehydroepiandrosterone, probucol, vitamin E, hydroxytoluene, carvidilol, α-lipoic acid, α-tocopherol, ubiquinone, phylloquinone, β-carotene, meanadione, glutamate, succinate, acetyl-L-carnitine, co-enzyme Q, lazeroids, polyphenolic flavonoids, homocysteine, menaquinone, idebenone, dantrolene – $(CH_2)_n[XCH_2)_n]NH_2$ - wherein n = 3-6 and X = nitrogen, sulfur, phosporous or carbon, or

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heterocycle wherein R_5 and R_6 taken together are $-(CH_2XCH_2)_n-$ wherein n = 3-6 and X = nitrogen, sulfur, phosporous or carbon.

M, n, and p may be the same or different and are bridging groups of variable length from 3-12 carbons.

X_1 and X_2 may be the same or different and are nitrogen, sulfur, phosporous or carbon.

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